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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/523,066 03/10/00 TULLY

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EXAMINER

FORMAN, B

ART UNIT

PAPER NUMBER

1655

DATE MAILED:

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/523,066

Applicant(s)

TULLY ET AL.

Examiner

BJ Forman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 May 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 1-10 and 16-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11-15 24-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

1. This action is in response to papers filed 21 May 2001 in Paper No. 9 in which claims 11 and 24 were amended. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action of Paper No. 7 dated 20 November 2000 under 35 U.S.C. 112, second paragraph, § b - d and g - i are withdrawn in view of the amendments. The previous rejections under 35 U.S.C. 103(a) are withdrawn in view of the publication date of the Luo et al. reference. All of the arguments have been thoroughly reviewed and are discussed below. New grounds for rejection are discussed.

Currently claims 11-15 and 24-26 are under prosecution.

2. Applicant's election with traverse of Group II, Claims 11-15 and 24-26 in Paper No. 9 is acknowledged. The traversal is on the grounds(s) that the inventions of Groups I and II are related and restriction is only required when the invention are independent and distinct. This is not found persuasive because dependent inventions may be properly restricted if they are distinct. As discussed in MPEP 803, one of the two criteria for requirement of restriction is that the "inventions must be independent (see MPEP 802.01, 806.04, 808.01) or distinct as claimed". Accordingly, the demonstration of distinctness of the inventions is sufficient grounds for restriction. As stated in MPEP 802.01 "(t)he law has long been established that dependent inventions (frequently termed related inventions) such as those used for illustration above may be properly divided if they are, in fact "distinct" inventions, even though dependent".

Applicants further argues that it would not be undue burden to examine the claims of all groups I and II. However, it is maintained that undue burden would be required to examine the claims of groups I along with claims of group II as evidenced by the fact that the claims of groups I and II have acquired a separate status in the art as recognized by their divergent subject matter and because a search of the subject matter of invention I is not co-extensive with a search of inventions II i.e. a search of the invention of Group I would encompass

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extensive search of all non-human animals not encompassed by the search of invention of Group II and the search of the invention of Group II encompasses extensive *Drosophila*-specific search not encompassed by the search of the invention of Group I.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 11-15 and 24-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 11-15 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete in Claim 11 for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps reciting "conditions appropriate" for training *Drosophila* to induce transcription-dependent memory and the steps reciting "condition insufficient" for training *Drosophila* to induce transcription-dependent memory. It is suggested that Claim 11 be amended to recite the missing steps (Specification, page 10, lines 2-21).

e. Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps reciting "conditions sufficient to induce transcription-independent memory but not transcription-dependent memory. It is suggested that Claim 14 be amended to recite the missing steps (specification, page 10, lines 2-21).

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f. Claims 24-26 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete in Claim 24 for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps reciting "conditions appropriate" for training *Drosophila* to induce transcription-dependent. It is suggested that Claim 24 be amended to recite the missing steps (Specification, page 10, lines 2-21).

Response to Arguments

5. Applicant argues that the "conditions appropriate" for training *Drosophila* to induce transcription-dependent memory formation refers to experimental conditions used in within the specification i.e. spaced training protocols and because other conditions for training could be determined using art-known methods and therefore the recitation "conditions appropriate" is not indefinite because one skilled in the art would understand the metes and bounds of the claim. This argument is not found persuasive because although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Additionally, this argument is not found persuasive because it has not basis i.e. no examples or explanation of what other conditions or methods are known in the art or what art-know method would be used to determine the conditions/methods. It is suggested that the claims be amended to clarify e.g. recite the steps for training (Specification, page 10, lines 2-12) or to recite are treated to induce transcription-dependent memory formation".

Applicant argues that "conditions insufficient" for training *Drosophila* to induce transcription-dependent memory refer to experimental conditions that are used to induce transcription-independent memory described in the specification and therefore when read in light of the specification, the metes and bounds of the claims are not indefinite. This argument is not found persuasive because although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Additionally, the argument is not found persuasive because it is unclear whether the *Drosophila* are treated or merely not treated so as to induce transcription-dependent memory formation and therefore the metes and bounds of the claims are undefined. It is suggested that the claims be amended to clarify e.g. recite the steps for training (Specification, page 10, lines 2-12) or to recite "are treated to induce transcription independent memory formation".

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 11-15 and 24-26 are rejected under 35 U.S.C. 103(a) as being obvious over Yin et al. (Cell, 1994, 79: 49-58) in view of Ramsey, G. (Nature Biotechnology, 1998, 16: 40-44) and Tully et al. (U.S. Patent No. 5,929,223, filed 7 October 1994).

Regarding Claim 11, Yin et al. teach a method of identifying a gene involved in transcription-dependent memory comprising: training *Drosophila* to induce transcription-dependent memory formation in said *Drosophila* i.e. spaced training, (page 50, last paragraph—page 51-first paragraph); extracting RNA from head tissue of said trained *Drosophila*; hybridizing the RNA to DNA sequences via Northern Blot from a gene of the *Drosophila* genome i.e. dCREB2-b cDNA, under conditions appropriate for hybridization wherein a signal is produced upon hybridization and detecting the signal produced (page 56, last paragraph) and performing a statistical comparison between the signal detected and a signal detected in a control (page 51, left column, last line-right column, first paragraph). Yin et al. teach training control *Drosophila* under conditions insufficient to induce transcription-dependent memory i.e. massed training (page 55, right column. second full paragraph) and performing statistical comparisons between the trained *Drosophila*. Yin et al. also teach a comparison of hybridization signal between *Drosophila* trained to induce transcription-dependent memory and *Drosophila* trained insufficiently to induce transcription dependent memory i.e. in the absence of training (page 50, last paragraph and Fig. 1). Yin et al. teach that the cAMP signal transduction pathway is critically involved with memory events and the

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pathway involves numerous cAMP response genes including transcription factors and they teach that drugs that interfere with transcription or translation disrupt memory. These teachings suggest that memory events require de novo gene expression and that numerous genes are involved with the memory events (page 79, left column, last paragraph-right column first full paragraph) and while they teach hybridization via Northern Blot to compare expression, they do not teach synthesizing DNA probes from the extracted RNA and exposing the DNA probes to microarray chips containing DNA sequences from genes of the *Drosophila* genome. However, microarrays comprising DNA sequences derived from extracted RNA was well known in the art at the time the claimed invention was made as taught by Ramsey. Specifically, Ramsey teaches a method to identify a gene or genes involved in transcription-dependent response comprising extracting RNA, synthesizing labeled cDNA probes from the RNA, hybridizing the DNA probes to microarray chips, detecting the signal produced, and performing a statistical comparison between the experimental and control (page 41, left column, last paragraph-right column) and they teach the method has been used in numerous model organisms e.g. plants, yeast, *S. cerevisiae*, *S. pneumoniae*, *E. coli* and has proven useful for large-scale, rapid identification of expression-specific genes (page 41, left column, last paragraph) wherein the array method was 10 time more sensitive than Northern Blots (page 41, right column last paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the northern blot gene identification of Yin et al. with the microarray identification exhibiting 10 fold sensitivity when compared to Northern Blots as taught by Ramsey wherein multiple response-specific genes are identified for the expected benefit of large-scale, rapid identification of expression-specific genes as taught by Ramsey (page 41, left column, last paragraph).

Regarding Claim 12, Yin et al. teach the method wherein transcription-dependent memory formation is long term memory formation (page 49, last paragraph-page 50, right column first full paragraph).

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Regarding Claim 13, Yin et al. teach the method wherein transcription-dependent memory formation is induced using a spaced training protocol (page 50, last paragraph—page 51, first paragraph). Additionally, Yin et al. teach the conditions of a massed training protocol (page 55, right column, first full paragraph, lines 24-29). Yin et al. do not teach the method wherein the hybridization signals from the spaced trained and massed trained *Drosophila* are compared. However, Tully et al. teach a similar method comprising: training two groups of *Drosophila*, one under conditions to induce transcription-dependent memory and a second under condition insufficient to induce transcription-dependent memory, extracting RNA from head tissue of both groups, hybridizing the RNA to DNA sequences from genes of the *Drosophila* and comparing the hybridization signals between the two groups (Column 25, lines 6-30). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the RNA analysis of Yin et al. wherein hybridization signals from trained and untrained *Drosophila* are compared to further compare hybridization signals from *Drosophila* following the different training protocols as taught by Tully et al. for the obvious benefit of analyzing training-specific expression to thereby identify memory-specific expression.

Regarding Claim 14, Yin et al. teach the conditions sufficient to induce transcription-independent memory formation but not transcription-dependent memory formation i.e. massed training (page 55, right column, first full paragraph, lines 24-29).

Regarding Claim 15, Yin et al. teach transcription-independent memory formation is induced using a massed training protocol (page 55, right column, first full paragraph, lines 24-29).

Regarding Claim 24, Yin et al. teach a method of identifying a gene involved in transcription-dependent memory comprising: training *Drosophila* to induce transcription-dependent memory formation in said *Drosophila* i.e. spaced training, (page 50, last paragraph—page 51—first paragraph); extracting RNA from head tissue of said trained *Drosophila*; exposing the RNA to DNA sequences from a gene of the *Drosophila* genome i.e.

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dCREB2-b cDNA, under conditions appropriate for hybridization wherein a signal is produced upon hybridization, detecting the signal produced, comparing the signal to the signal from control *Drosophila* (page 56, last paragraph) and performing a statistical comparison between the signal detected and a signal detected in a control (page 51, left column, last line-right column, first paragraph) Yin et al. teach that the cAMP signal transduction pathway is critically involved with memory events and the pathway involves numerous cAMP response genes including transcription factors and they teach that drugs that interfere with transcription or translation disrupt memory. These teachings suggest that memory events require de novo gene expression and that numerous genes are involved with the memory events (page 79, left column, last paragraph-right column first full paragraph) and while they teach hybridization via Northern Blot to compare expression, they do not teach synthesizing DNA probes from the extracted RNA and exposing the DNA probes to microarray chips containing DNA sequences from genes of the *Drosophila* genome they do not teach synthesizing DNA probes from the extracted RNA and exposing the DNA probes to microarray chips containing DNA sequences from genes of the *Drosophila* genome. However, microarrays comprising DNA sequences derived from extracted RNA was well known in the art at the time the claimed invention was made as taught by Ramsey. Specifically, Ramsey teaches a method to identify a gene or genes involved in transcription-dependent response comprising extracting RNA, synthesizing labeled cDNA probes from the RNA, hybridizing the DNA probes to microarray chips, detecting the signal produced, and performing a statistical comparison between the experimental (page 41, left column, last paragraph-right column) and they teach the method has been used in numerous model organisms e.g. plants, yeast, *S. cerevisiae*, *S. pneumoniae*, *E. coli* and has proven useful for rapid identification of expression-specific genes (page 41, left column, last paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the northern blot gene identification of Yin et al. with the microarray identification exhibiting 10 fold sensitivity when compared to Northern Blots as taught by

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Ramsey wherein multiple response-specific genes are identified for the expected benefit of large-scale, rapid identification of expression-specific genes as taught by Ramsey (page 41, left column, last paragraph).

Regarding Claim 25, Yin et al. teach the method wherein said transcription-dependent memory formation is long term memory formation i.e. spaced training (page 51, left column, first paragraph).

Regarding Claim 26, Yin et al. teach the method wherein said transcription-dependent memory formation is induced using a spaced training protocol (page 51, left column, first paragraph).

Response to Arguments

Applicants argue that Yin et al. and Tully et al. do not teach or suggest use of microarray chips to identify genes involved in transcription-dependent memory formation and they do not teach use of a statistical comparison between signal detected from a control microarray chip and experimental microarray chip. This argument is considered, but mooted in view of the withdrawn rejection and new grounds for rejection discussed above.

Conclusion

8. No claim is allowed.

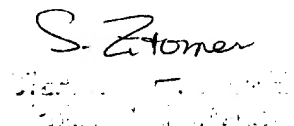
9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:45 TO 4:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



BJ Forman, Ph.D.
July 12, 2001



S. Zomer
Supervisor